REMARKS

This is in response to the Office Action mailed June 18, 2002, in the above-referenced application. Claims 1-3, 5, 6, 10, 12-15, 19-35, and 37-46 stand rejected. Claims 1, 6, 10, 13, 22, 23, 25-27, 32, 33, 35, 37, and 38 have been amended. Claims 3, 5, 14, 15, 19-21, 24, 30, 31, and 39- 46 have been cancelled. Claims 1, 2, 5, 6, 10, 12, 13, 22, 23, 25-29, 32-35, 37, and 38 remain pending.

Claims 13-15 and 21-23 are rejected under 35 USC § 102(a) or 102(b) as anticipated by, or alternatively, under 35 USC § 103 as obvious over WO 94/26872 to Davies. Applicant offers the following comments.

Davies is directed to the application of a sol-gel to a substrate, such as a quartz substrate, among others. The Office argues that during sintering, silicon from the quartz would permeate into the sol. Following the Davies procedure, the resultant film would incorporate a gradient of silicon during sintering, such that the film would include areas with different concentrations of silicon at different locations therein.

Claims 13 and 23 are amended to depend from Claim 1, which recites the bioactive composition as a powder or bulk material, support for which is given on page 6, line 8 of the specification. Claims 14, 15, and 21 are cancelled. The powder or bulk material recited in Claim 1 stands in contrast to the film coating taught by the Davies reference. The Davies reference does not teach or suggest the claimed method of making a bulk or powder composition of the instant claims.

Further, Claim 13 recites that stabilizing entities are uniformly distributed throughout an entire hydroxyapatite substance. Davies method results in a gradient of silicon within a hydroxyapatite film. Figures 5a, 5b, and 5c of the present application present analytical data on the concentrations of the film components, including silicon, at different locations of a film prepared by sintering hydroxyapatite on a quartz substrate. See page 17, lines 5-11. As demonstrated, films which are sintered upon quartz substrates, such as done by Davies, have

areas of different silicon concentrations at different locations within the film, such that the silicon is not uniformly distributed.

Still further, as recited in Claim 13 (from which Claim 22 depends), the hydroxyapatite precursor material of the invention is uniformly doped with stabilizing entities and thereafter the uniformly doped hydroxyapatite is sintered. The resultant tricalcium phosphate composition includes stabilizing entities uniformly distributed throughout. This process is in stark contrast to the Davies reference, which teaches sintering of a hydroxyapatite film to a quartz substrate with the concurrent doping of silicon. Davies does not teach or suggest doping a hydroxyapatite substance with stabilizing entities prior to sintering of the hydroxyapatite material.

In summary, the claimed invention recites a bulk or powder that incorporates uniformly distributed stabilizing entities prior to sintering. In contrast, the Davies procedure teaches a film that incorporates a gradient of silicon during sintering. Therefore, the invention recited in Claims 13, 22, and 23 is not taught or suggested by the Davies reference.

Claims 1-3, 5, 6, 12-15, 21, 23, 24 and 31-34 are rejected under 35 USC § 102(b) as anticipated by U.S. Patent No. 4,983,182 to Kijima et al. Applicants have added a Markush group to list the specific stabilizing entities utilized by the claimed invention in Claim 1. All other claims rejected in view of Kijima have been amended to depend from Claim 1. The recited claims are neither taught nor suggested by the Kijima reference.

Claims 1-3, 5, 6, 12-15, 19, 21-25, 31, 32, 34, 38-41, 43, and 45 stand rejected in view of Ruys. The amendments to Claims 1 and 13, the amended dependency of Claims 6, 23, 25, and 32, and the cancellation of Claims 3, 5, 14, 15, 19, 21, 24, 31, and 39-46 have obviated the rejection. The recited claims are neither taught nor suggested by the Ruys reference.

Claims 27-30, 35, 37, 42, and 46 are rejected in view of Ruys in combination with Davies, and Claim 44 is rejected in view of Ruys in combination with Kijima. In view of the above amendments, the rejections have been obviated.

The rejections of record having been addressed in full in the foregoing, Applicants respectfully submit that this application is now in condition for allowance, which action is

respectfully solicited. Should the Examiner have any questions regarding the foregoing, it is respectfully requested that he contact the undersigned at his convenience to expedite examination.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Commissioner for Patents, Washington, DC 20231, on December 18, 2002.

Tamara Stevens

Version with Markings to Show Changes Made:

1. (Four times amended) A bioactive artificial sintered composition for [consistently] supporting bone cell activity, said composition comprising:

a powder or bulk material of stabilized insoluble tricalcium phosphate wherein the tricalcium phosphate is stabilized with [uniformly stabilized tricalcium phosphate having] stabilizing entities [distributed] uniformly throughout the entire composition, and wherein said uniformly stabilized tricalcium phosphate is resorbable by osteoclasts and promotes secretion of mineralized bone matrix by osteoblasts [insoluble in physiological fluids],

wherein said stabilizing entities are selected from the group consisting of silicon entities, aluminum entities, barium entities, titanium entities, germanium entities, chromium entities, vanadium entities, niobium entities, boron entities and mixtures thereof.

6. (Twice amended) A composition as claimed in claim 1 [5], wherein said stabilizing entities are provided as a [in] solution.

10. (Twice amended) The composition as claimed in claim 6, wherein said stabilizing entities are a solution [A bioactive artificial sintered composition for providing a morphology capable of consistently supporting bone cell activity thereon, said composition comprising stabilized calcium phosphate phases developed by the conversion of a hydroxyapatite substance in the presence] of tetrapropyl orthosilicate [stabilizing entities at sintering temperatures into insolubilized and stabilized tricalcium phosphate].

13. (Twice amended) A process for making the composition of Claim 1, said process comprising:

[stabilizing an artificial sintered composition of calcium phosphate phases having a morphology suitable for supporting bone cell activity, said process comprising substantially uniformly]

doping and mixing a hydroxyapatite substance with a composition of stabilizing entities to uniformly distribute said stabilizing entities throughout said entire hydroxyapatite substance; and sintering said [substantially] uniformly doped hydroxyapatite substance; wherein sintering converts at least a portion of said [substantially] uniformly doped hydroxyapatite substance into primarily [uniformly stabilized] alpha tricalcium phosphate [which is insoluble in physiological fluids and said stabilizing entities stabilize the formed alpha tricalcium phosphate within the phosphate phases].

22. (Once amended) The [A] process of [as claimed in] claim 13, wherein sintering [of the hydroxyapatite substance] is done at temperatures of about 900°C to 1100°C.

23. (Once amended) The composition of claim 1, where said composition is provided as a [A sintered artificial] microporous polycrystalline structure [for supporting bone cell activity, said structure comprising sintered stabilized calcium phosphate phases having a globular surface morphology of loosely interconnected rounded granules with interconnected micropores in said structure, wherein said stabilized calcium phosphate phases are developed by the conversion of a hydroxyapatite substance doped with added stabilizing entities at sintering temperatures into insolubilized and stabilized tricalcium phosphate].

25. (Three times amended) The composition [A polycrystalline structure] of claim 23 [24], wherein said structure has said globular morphology of Figure 14.

26. (Once amended) The composition [A polycrystalline structure] of claim 25, wherein said morphology comprises rounded granules with [have] a lateral dimension of about [in the range of] 0.5 to 1μm.

27. (Three times amended) An implantable calcified bone matrix comprising:

a) the composition of claim 1 forming a structure for supporting said bone matrix; and [a structure for supporting said matrix;]

b) [a layer of uniformly stabilized tricalcium phosphate phases developed by the conversion of a hydroxyapatite substance uniformly doped with stabilizing entities at sintering temperatures into uniformly stabilized tricalcium phosphate where said stabilizing entities insolubilize and stabilize the tricalcium phosphate phases;

c) a boundary layer deposited by osteoblasts cultured on said layer of stabilized tricalcium phosphate phases; and

d)] a [mineralizing collagenous] calcified bone matrix secreted by [such cultured] osteoblasts on said structure.

32. (Once amended) The composition of [A bulk ceramic microporous structure as claimed in] claim 23 [30], wherein said composition [structure] has an internal macroporosity.

33. (Once amended) An implantable device comprising the [coated with the sintered] composition of claim 1.

35. (Twice amended) A method for the culturing of functional bone cells, said method comprising: [;]

applying a suspension of bone cells in physiological media to the [at a suitable physiological temperature to an artificial sintered] composition of claim 1 provided as a substrate.

37. (Twice amended) A method for the *ex vivo* engineering of a mineralized collagenous implant [matrix], the method comprising the steps of :

a) providing the composition of claim 1 as a bulk material; [an artificial stabilized composition having a globular surface morphology of loosely interconnected rounded granules with interconnected micropores,]

b) applying a suspension of osteoblasts on said composition and incubating for a time sufficient for said osteoblasts to secrete mineralized collagenous bone matrix on said bulk material; and [in physiological media on the composition,]

[incubating the mineralized collagenous bone matrix secreted by the osteoblasts from the culture; and]

c) implanting the product of step (b) [isolated collagenous bone matrix] in a patient.

38. (Once amended) The [A] composition of [as claimed in] claim 1, wherein said stabilizing entities are silicon [entities].